General

Guideline Title

Practice parameter: thymectomy for autoimmune myasthenia gravis (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology.

Bibliographic Source(s)

Gronseth GS, Barohn RJ. Practice parameter: thymectomy for autoimmune myasthenia gravis (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000 Jul 12;55(1):7-15. [44 references]

Guideline Status

This is the current release of the guideline.

The American Academy of Neurology (AAN) reaffirmed the currency of the guideline in August 2014.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Each practice recommendation is rated based on the strength of the evidence. Definitions of the strength of the recommendations (standard, guideline, practice option, practice advisory) and quality of the evidence (Class I-Class III) are presented at the end of the Major Recommendations field.

Conclusions

After systematically reviewing the controlled but nonrandomized studies describing outcomes in myasthenia gravis patients undergoing and not undergoing thymectomy the authors found:

positive associations in most studies between thymectomy and myasthenia gravis remission and improvement (median relative rate of medication-free remission, 2.1; asymptomatic, 1.6; improvement, 1.7)
confounding differences in baseline characteristics of prognostic importance between thymectomy and nonthymectomy patient groups in all studies
persistent positive associations between thymectomy and improved myasthenia gravis outcomes after controlling for single confounding variables such as age, gender, and severity of myasthenia gravis
conflicting associations between thymectomy and improved myasthenia gravis outcomes in studies controlling for multiple confounding variables simultaneously

The authors cannot determine from the available studies whether the observed association between thymectomy and improved myasthenia gravis outcome was a result of a thymectomy benefit or was merely a result of the multiple differences in baseline characteristics between the surgical and nonsurgical groups. Based on these findings, the authors conclude that the benefit of thymectomy in non-thymomatous autoimmune myasthenia gravis has not been established conclusively.

Practice Recommendation

For patients with nonthymomatous autoimmune myasthenia gravis, thymectomy is recommended as an *option* to increase the probability of remission or improvement (Class II).

Definitions:

Classification of Evidence

Class I: Evidence provided by one or more well-designed randomized controlled trials, including overviews (meta-analyses) of such trials.

Class II: Evidence provided by well-designed observational studies with concurrent controls (e.g., caseâ€“control and cohort studies).

Class III: Evidence provided by expert opinion, case series, and studies with historical controls.

Strength of Recommendations

Standards: A principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical question or overwhelming Class II evidence when circumstances preclude randomized clinical trials).

Guidelines: A recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence).

Practice option: A strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion).

Practice advisory: A practice recommendation for emerging and/or newly approved therapies or technologies based on evidence from at least one Class I study. The evidence may demonstrate only a modest statistical effect or limited (partial) clinical response, or notable costâ€“benefit questions may exist. Substantial (or potential) disagreement among practitioners or between payers and practitioners may exist.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Nonthymomatous autoimmune myasthenia gravis

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Neurology

Intended Users

Physicians

Guideline Objective(s)

To develop evidence-based recommendations for clinicians considering thymectomy for patients with nonthymomatous autoimmune myasthenia gravis by performing a systematic review and analysis of the literature

Target Population

Patients with nonthymomatous autoimmune myasthenia gravis

Interventions and Practices Considered

Thymectomy

Major Outcomes Considered

- Survival (taking into account perioperative mortality)
- Improvement since diagnosis
- Asymptomatic on or off medication (remission)
- Asymptomatic off medication (medication-free remission)

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Original Guideline

The authors searched the National Library of Medicine's Medline database from 1966 to February 1998 using the medical subject headings "myasthenia gravis" (restricted to the surgery subheading) and "thymectomy". To identify articles published before 1966, or missed by our original search strategy, we reviewed the references of the identified articles.

2014 Reaffirmation

Medline was searched from 2010 July 10 to 2014 August 9 for the terms “myasthenia gravis” and “thymectomy.” The included controlled studies described outcomes in myasthenia gravis patients treated with and without thymectomy. Class III (uncontrolled case studies) and patients with thymomas were excluded from the analysis.

Number of Source Documents

310 retrieved

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions for classification of evidence:

Class I. Evidence provided by one or more well-designed randomized controlled trials, including overviews (meta-analyses) of such trials.

Class II. Evidence provided by well-designed observational studies with concurrent controls (e.g., caseâ€“control and cohort studies).

Class III. Evidence provided by expert opinion, case series, and studies with historical controls.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Within a given controlled (Class II) study, the authors describe the therapeutic effect of thymectomy by comparing the rate myasthenia gravis patients receiving thymectomy achieved desirable outcomes with the rate myasthenia gravis patients not receiving thymectomy achieved desirable outcomes. The nonrandomized nature of Class II studies often introduces differences in the baseline characteristics of the thymectomy and non-thymectomy patient groups that can effect myasthenia gravis outcomes independent of thymectomy. To the extent possible, the authors adjust for these confounding differences in baseline prognostic characteristics. In the absence of randomized controlled trials, such adjustments are critical for estimating the actual therapeutic effect, if any, of thymectomy. (Note: Class III studies were excluded from consideration.)

From the controlled studies describing outcomes, the following characteristics were abstracted: method and setting of cohort assembly, years during which patients were enrolled in the cohort, number of subjects assembled, duration of follow-up, proportion of subjects lost to follow-up, and the thymectomy techniques employed.

Because of reported associations with myasthenia gravis outcomes, the authors also extracted the following study population characteristics: proportion of patients younger than 50 years at the time of diagnosis of myasthenia gravis, proportion of female patients with more severe myasthenia gravis at the time of diagnosis (defined by Osserman's grade 2b, 3, or 4), and the proportion of patients with strictly ocular myasthenia at the time of diagnosis.

Thymectomy in patients with thymoma has benefits other than myasthenia gravis treatment. Therefore, patients with thymoma were excluded from the analysis.

In reviewing each study the authors considered the following myasthenia gravis outcomes: survival (taking into account perioperative mortality), improvement since diagnosis, asymptomatic on or off medication, and asymptomatic off medication (i.e., medication-free remission).

Ideally, controlled studies of thymectomy in myasthenia gravis patients report outcomes using time-to-outcome (survival) techniques. Survival techniques account for the differences in the duration of follow-up and changes in outcomes over time. Unfortunately, most controlled studies of thymectomy in myasthenia gravis simply report the proportion, or crude rate, of patients achieving an outcome over the studyâ€™s follow-up period. Crude outcome rates vary with the duration of follow-up of the study. Within a given study, however, crude outcome rates of the thymectomy and nonthymectomy patient groups can be compared when the patient groups have similar follow-up durations.

To compare the crude rates within a given controlled study, the authors calculated the relative rate by dividing the thymectomy patient groupâ€™s crude rate of achieving the outcome by the nonthymectomy patient groupâ€™s crude rate of achieving the outcome using the formula presented in table 1 of the guideline document.

The authors also calculated the 95% confidence interval of these relative rates. Calculation of the relative outcome rates in this manner compensates for differences in follow-up duration between controlled studies, and allows the analysis of the results of all controlled thymectomy

myasthenia gravis studies.

In studies providing sufficient information, the authors re-calculated the relative rates of outcomes after controlling for potential confounding variables of age, gender, and severity of myasthenia. The authors used Wilcoxonâ€™s test to determine significance of the changes in relative rates measured after controlling for these variables.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

2014 Reaffirmation

An author conducted a literature search using the same criteria as presented in the original guideline. Because the guideline recommendations would not changes given the new literature available, the committee voted to reaffirm the guideline, stating that the conclusions and recommendations are still valid.

Rating Scheme for the Strength of the Recommendations

Definitions for the Strength of Recommendations:

Standards: A principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical question or overwhelming Class II evidence when circumstances preclude randomized clinical trials).

Guidelines: A recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence).

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Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Numerous individuals, American Academy of Neurology (AAN) Sections, and organizations reviewed drafts of this practice parameter, including: the Muscular Dystrophy Association; Society of Thoracic Surgeons; Myasthenia Gravis Foundation; AB Baker Section; Autonomic Nervous System Section; Government Services Section; Neuromuscular Section; Sleep Section; and Epilepsy Section.

The practice parameter was approved by the American Academy of Neurology Quality Standards Subcommittee on October 8, 1999, by the Practice Committee on January 15, 2000, and by the American Academy of Neurology Board of Directors on February 26, 2000.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

For patients with nonthymomatous autoimmune myasthenia gravis, thymectomy may increase the probability of remission or improvement.

Potential Harms

Thymectomy complications

Eleven of the studies reviewed here reported thymectomy-related mortality. Perioperative mortality rates were higher in patients undergoing thymectomy before 1970, with commonly reported rates between 5 and 15%. After 1970, reported mortality rates in the studies reviewed here were consistently less than 1%. Common morbidities include acute respiratory failure from crisis in 6%, infection in 11%, and permanent nerve injury (usually the recurrent laryngeal or phrenic nerve) in 2% of patients. Lower complication rates are reported with newer thymectomy techniques such as video-assisted thoracic surgery.

Qualifying Statements

Qualifying Statements

This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

All currently published studies have serious methodological flaws that prevent definitive conclusions regarding the benefit of thymectomy. These flaws include:

- the absence of randomized allocation to thymectomy and nonthymectomy treatment groups;
- the absence of standardized, masked outcome determinations; and
- confounding differences in enrollment year, age, gender, disease duration, and severity in surgical and nonsurgical groups.

Because of these serious limitations, a well-designed controlled trial is essential.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2000 Jul (reaffirmed 2014 Aug 9)

Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

Source(s) of Funding

American Academy of Neurology (AAN)

Guideline Committee

Quality Standards Subcommittee

Composition of Group That Authored the Guideline

Committee Members: Gary Franklin, MD, MPH (Co-Chair); Catherine Zahn, MD (Co-Chair); Milton Alter, MD, PhD; Stephen Ashwal, MD; John Calverley, MD; Richard Dubinsky, MD; Jacqueline French, MD; Michael Greenberg, MD; Gary Gronseth, MD (facilitator); Deborah Hirtz, MD; Robert Miller, MD; James Stevens, MD, and William Weiner, MD

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

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This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

A list of American Academy of Neurology (AAN) guidelines, along with a link to this guideline, is available at the AAN Web site .

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 201 Chicago Avenue South, Minneapolis, MN 55415.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This summary was completed by ECRI on February 12, 2002. The information was verified by the guideline developer as of March 29, 2002. This information was reaffirmed by the guideline developer on July 10, 2010 and this summary updated by ECRI Institute on December 17, 2010. The currency of the guideline was reaffirmed by the developer in August 2014 and the summary was updated by ECRI Institute on December 22, 2015.

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